UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Chemical Safety and Pollution Prevention

MEMORANDUM

Date: Aug 1, 2012

SUBJECT: Common Triazole Metabolites: Updated Aggregate Human Health Risk Assessment to Address The Amended Propiconazole Section 3 Registration to Add Use on Sugarcane.

PC Codes: 600074 (1,2,4-Triazole), 600011 (Triazolylalanine), 600082 (Triazolylacetic Acid), 625618 (Triazolylpyruvic Acid)	DP Barcode: 403619
Decision No.: 451291	Registration No.: None
Petition Nos.: 1F7892	Regulatory Action: Amended Section 3
Assessment Type: Single Chemical, Aggregate	Registration Case No.: NA
TXR No.: None	CAS No.: Multiple
MRID No.: None	

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I. CONCLUSIONS

Based on conservative, health-protective assumptions, aggregate risk estimates associated with 1,2,4-triazole (T) and the conjugated triazole metabolites [i.e., combined residues of triazolylalanine (TA), triazolylacetic acid (TAA), and triazolylpyruvic acid (TP)] are below HED's level of concern. There are no human heath risk issues for these metabolites that would preclude the requested use of propiconazole.

II. ACTION REQUESTED

Update the aggregate human health risk assessments for T and the conjugated triazole metabolites to account for amended use on propiconazole.

III. BACKGROUND

In 2006, HED issued aggregate human health risk assessments for T and the conjugated triazole metabolites (M. Doherty, *et al.*, D322215, 7 FEB 06). Those assessments addressed a back-log of triazole use requests that had been held by the Agency pending resolution of various toxicological and exposure concerns for the common triazole metabolites. The findings of that assessment were that risk estimates for all exposure scenarios were below HED's level of concern. Since that time, a number of requests for new uses of triazole-derivative fungicides have been submitted to the Agency. As a result of these requests, new dietary exposure estimates have been made for T and combined residues of TA, TAA, and TP, and new aggregate exposure and risk estimates are necessary. Neither the toxicological information nor the non-dietary exposure estimates detailed in the 2006 memorandum have changed; thus the only alterations to the previous aggregate exposure and risk estimates are due to changes in the dietary exposure estimates. For complete hazard characterization and non-dietary exposure assessments for the common triazole metabolites, see the 2006 risk assessment.

IV. RESULTS/DISCUSSION

As noted above, the only revisions to the components of the previous aggregate exposure and risk estimates are to the dietary exposure estimates. For the common triazole metabolites, acute and chronic aggregate risks consist only of dietary (food + water) components and, therefore, are equivalent to the dietary risk estimates provided in the most recent dietary exposure assessment (T. Morton, D403618, July 31, 2012).

The revised aggregate estimates are summarized below for short- and intermediate-term scenarios for T (Tables 2 and 3, respectively). The conjugated triazole metabolites are formed in plants by the conjugation of 1,2,4-T to serine. The TA may then be further metabolized to form TAA and/or TP. Because of the nature of this process, HED has assumed that it occurs within the plant itself and not on leaf surfaces. Therefore, the residues are not available for dermal, hand-to-mouth, or object-to-mouth exposures and HED has not conducted a residential exposure assessment for the triazole conjugates. Residues of TA, TAA, and TP may occur in soil. 1,2,4-Triazole is more toxic than TA/TAA/TP and exposures to these via soil ingestion are unlikely to exceed those of 1,2,4-T. The assessment for soil ingestion of 1,2,4-T shows that risk estimates

are below HED's level of concern; therefore, risk estimates for soil ingestion of the conjugates will also be below HED's level of concern.

Table 1. Summary of Dietary (Food and Drinking Water) Exposure and Risk for the Common Triazole Metabolites Adding the Amended Use for Propiconazole.

Population Subgroup	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD*	Dietary Exposure (mg/kg/day)	% cPAD*	Dietary Exposure (mg/kg/day)	Risk
1,2,4-Triazole						
General U.S. Population	0.008282	28	0.001327	27	Not Applicable	Not Applicable
All Infants (< 1 year old)	0.012115	40	0.001843	37		
Children 1-2 years old	**0.023117**	**77**	**0.003832**	**77**		
Children 3-5 years old	0.018974	63	0.003064	61		
Children 6-12 years old	0.010992	37	0.001665	33		
Youth 13-19 years old	0.007222	24	0.001085	22		
Adults 20-49 years old	0.006609	22	0.001137	23		
Adults 50+ years old	0.005820	19	0.001073	22		
Females 13-49 years old	0.006747	22	0.001110	22		
Triazolylalanine + Triazolylacetic Acid+Triazolylpyruvic acid						
General U.S. Population	Not Applicable	Not Applicable	0.018547	21	Not Applicable	Not Applicable
All Infants (< 1 year old)			0.021851	24		
Children 1-2 years old			**0.058600**	**65**		
Children 3-5 years old			0.047124	52		
Children 6-12 years old			0.024837	28		
Youth 13-19 years old			0.015657	17		
Adults 20-49 years old			0.015272	17		
Adults 50+ years old			0.014323	16		
Females 13-49 years old	**0.079772**	**80**	0.014900	17		

* The values for the highest exposed population for each type of risk assessment are bolded.

Table 2. Short-term Aggregate Exposure and Risk Estimates for 1,2,4-Triazole.

Population Subgroup	Exposure Estimate, mg/kg/day[1]							Aggregate MOE[2]
	Dietary	Dermal (M/L/A)	Dermal (Post-Applic.)	Hand-to-Mouth	Object-to-Mouth	Soil Ingestion	Aggregate	
U.S. Population (total)	0.001327	0.00183	0.0051	N/A	N/A	N/A	0.008257	3600
All infants (< 1 year)	0.001843	N/A	0.0086	0.0041	0.0010	0.000019	0.015562	1900
Children 1-2 yrs	0.003832	N/A	0.0086	0.0041	0.0010	0.000019	0.017551	1700
Children 3-5 yrs	0.003064	N/A	0.0086	0.0041	0.0010	0.000019	0.016783	1800
Children 6-12 yrs	0.001665	N/A	0.0086	N/A	N/A	N/A	0.010265	2900
Youth 13-19 yrs	0.001085	0.00183	0.0051	N/A	N/A	N/A	0.008015	3700
Adults 20-49 yrs	0.001137	0.00183	0.0051	N/A	N/A	N/A	0.008067	3700
Adults 50+ yrs	0.001073	0.00183	0.0051	N/A	N/A	N/A	0.008003	3700
Females 13-49 yrs	0.001110	0.00183	0.0051	N/A	N/A	N/A	0.00804	3700

[1] Exposure estimates for dermal, hand-to-mouth, object-to-mouth, and soil ingestion are from J. Arthur, DP 322240, 12/9/05.
[2] Aggregate MOE = NOAEL (30 mg/kg/day) ÷ Aggregate Exposure Estimate (mg/kg/day). Level of Concern = 1000.

Table 3. Intermediate-term Aggregate Exposure and Risk Estimates for 1,2,4-Triazole.

Population Subgroup	Exposure Estimate, mg/kg/day			Aggregate MOE[2]
	Dietary	Soil Ingestion[1]	Aggregate	
U.S. Population (total)	0.001327	N/A	0.001327	11000
All infants (< 1 year)	0.001843	0.000019	0.001862	8100
Children 1-2 yrs	0.003832	0.000019	0.003851	3900
Children 3-5 yrs	0.003064	0.000019	0.003083	4900
Children 6-12 yrs	0.001665	N/A	0.001665	9000
Youth 13-19 yrs	0.001085	N/A	0.001085	14000
Adults 20-49 yrs	0.001137	N/A	0.001137	13000
Adults 50+ yrs	0.001073	N/A	0.001073	14000
Females 13-49 yrs	0.001110	N/A	0.001110	14000

[1] Soil ingestion estimates are from J. Arthur, DP 322240, 12/9/05
[2] Aggregate MOE = NOAEL (15 mg/kg/day) ÷ Aggregate Exposure Estimate (mg/kg/day). Level of Concern = 3000.